HTAi Virtual Conference, June 2021: Innovation through HTA

Panel Session Report

Digital Health Interventions/Technologies: Evidence Needed, Methods and Assessment for Policy Decisions

Key points

Digital health is the field of knowledge and practice associated with the development and use of digital technologies to improve health care and health, encompassing mobile health, telemedicine, eHealth, digital diagnostics and digital therapeutics. With the rapid digitization of health-related data comes the ability to draw on data science methodologies such as artificial intelligence to develop personalised medicine approaches.

Digital health technologies come with the promise of system efficiencies and improved outcomes, but it is often unclear whether they will deliver on these promises. Consequently, evaluation is needed but health technology assessment (HTA) is currently underused.

The use of digital technologies to improve the efficiency of pharmaceutical research and development, and deliver Drug+ approaches, will continue at a fast pace. Reasonable and consistent approaches to validation and assessment are needed across geographies and decision-makers.

When evaluating digital health technologies, it is important to use participatory approaches that involve staff and users to understand the clinical problem, in evaluation and in implementation. Research designs should be fit-for-purpose given the expected impact of the technology, so RCTs of clinical outcomes may not always be necessary. More emphasis should be placed on patients' perspectives, such as empowerment to self-manage their condition, improved activities of daily living or reduced clinic travel times.

Traditional HTA methods can be used to assess bias, generalizability and uncertainties associated with digital health technologies, but new skills and methods are needed to understand issues such as those relating to the use of technologies with adaptive algorithms within the health care systems.

HTA of digital health technologies needs to address not only outcomes, but also structure and processes. Collaboration needs to be enhanced to develop methodologies that take account of the diversity of technology readiness and infrastructure limitations in different health systems, particularly those in low-and-middle income countries.

Although digital technologies are being introduced rapidly into health care systems, there is no systematic assessment of their value. Moreover, traditional study designs and methods to assess the value of health technologies may not always be appropriate for digital technologies. Therefore, HTA needs to be developed further to deliver efficient primary research methods and secondary assessment approaches to evaluate digital health technologies in a manner that is fit-for-purpose for the technology, the health system and focuses on patient benefit.

Contents

Glossary

AdHopHTA	Adopting Hospital-based HTA
AI	Artificial Intelligence
CE	Conformité Européenne
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
EU	European Union
EUnetHTA	European Network for HTA
HTA	Health Technology Assessment
HTAi	Health Technology Assessment international
ML	Machine Learning
NICE	National Institute for Health and Care Excellence
PRO	Patient Reported Outcome
QALY	Quality Adjusted Life Year
R&D	Research and Development
RCT	Randomized-Controlled Trial
RWD	Real-World Data
US	United States (of America)
UPDRS	Unified Parkinson's Disease Rating Scale

About HTAi

Health Technology Assessment international (HTAi) is the global scientific and professional society for all those who produce, use, or encounter HTA. HTAi has members from over 65 countries and embraces all stakeholders, including researchers, agencies, policy makers, industry, academia, health service providers, and patients/consumers. HTAi is the neutral forum for collaboration and the sharing of leading information and expertise. This panel was judged by three reviewers and selected for presentation at the 2021 annual meeting by the International Scientific Program Committee.

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Digital Health Interventions – Evidence Needed, Methods and Assessment for Policy Decisions

1. Introduction

Dr Laura Sampietro-Colom, Deputy Director Innovation and Head of Evaluation of Innovation and New Technologies, Hospital Clínic Barcelona, Spain

Dr Sampietro-Colom gave an introduction to this HTAi 2021 panel reflecting on the accelerated provision of digital health technologies during the Covid-19 pandemic, perhaps by at least two years. Digital health technologies is a wide-ranging term and in the pandemic they have been used in the following ways:

- artificial intelligence, for example to detect Covid-19 via chatroom discussions
- telemedicine to create virtual hospitals
- contact tracing apps
- health apps to deal with consequences, for example mental health issues
- wearables to act as an early warning system for viral illness
- 3-D printing for valves that were not available due to a break in the supply chain
- robots used for a variety of purposes.

Pandemics prompt focus on digital and virtual care and the global digital health market has grown substantially. In a 2020 survey it was estimated that by 2025, 12% of healthcare expenditure would be on digital products and services. This was anticipated due to the wide-ranging promises of digital technologies in relation to cost savings, efficiencies, breaking down silo working, stakeholder integration, provision of meaningful data and analytics, e.g., to monitor performance and to deliver a more agile, learning health system. However, these promises need to be scrutinized as all that glitters is not gold. Key questions include:

- Can digital technologies help in developing new treatments and improving market access to ensure the right medicines are given to the right patients?
- What are the best methods, processes and outcomes to advise policy makers and clinical decision-makers?
- Is there a need to innovate HTA for digital health technologies?
- In a global context, with different evolution of digital technologies, can we harmonize approaches?

These questions were discussed in this panel from the context of the HTA community, beginning with a poll for the audience.

Poll question 1 with audience
Are we ready to assess digital health technologies with our current HTA methods?
67% No, 33% Yes.

2. Digitalization in Healthcare and Research: Views from Big Pharma Research and Development

Eric Genevois-Marin, Vice President and Global Head of Research and Development Data and Data Science, Sanofi

Mr Genevois-Marlin presented insights into the use of data and analytics in research and development (R&D) in the pharmaceutical sector, with a focus on activities at Sanofi.

Potential to improve efficiency in R&D

Developing a new medicine is a long, costly and risky process that may yield a treatment that does not fully satisfy the needs of the health system and patients. In recent years, these aspects have been worsening despite the long-standing concerns raised by the pharmaceutical sector.

The key questions that need to be considered to improve the efficiency and effectiveness of medicine's R&D include:

- How can novel target/diseases be optimally identified?
- How can we understand patients' treatment patterns and behaviors better?
- What is the best endpoint for: internal R&D decision making, for patients, for regulators, for payers?
- How can clinical trial designs be optimized to improve their probability of success?
- How can the value of a molecule be optimized?

As R&D has always made decisions about a medicine's development based on accumulating data, digital technologies offer important new opportunities that could be at the heart of innovating R&D to address these questions and make it more efficient. For example:

- Use of Artificial Intelligence (AI) is expanding across all areas of pharmaceutical R&D to maximize use of data, images, text and other information to diagnose, understand, predict, personalize and to automate.
- In early development, there is increasing use of clinical real-world data (RWD) enriched with –omics data to understand disease biology, find targets for medicines, understand patients' phenotypes, connect clinical outcomes with biology to determine causal relationships and discover potential new treatments.
- Digital biomarkers, including patient reported outcomes (PROs), can improve clinical trial convenience and be used as an effectiveness endpoint.
- Use of RWD could be expanded to understand disease, predict outcomes, design better trials and ultimately create external control arms (recognizing that quality, completeness and biases need to be addressed).
- Drug+App options could enhance the impact of a treatment by providing a digital health app that facilitates management of the disease, providing additional benefit to patients.

Examples

Three examples highlight how digital health technologies can contribute to pharmaceutical R&D in different diseases. These arise from experience in Sanofi, but are typical of the types of activities underway in other large pharmaceutical companies.

Example 1: Precision Medicine - finding the right patient for a medicine – seeking those that offer most benefit and avoid side effects.
In lung cancer it is important to identify patients who are positive to a specific antigen to optimize treatment. Traditionally this has been undertaken by human review of microscopic immunologic/histologic/chemistry images. The AI approach of Deep Learning has been applied to these images and successfully used to differentiate patients who would benefit from a treatment and those who would not. The AI could be also used with a companion diagnostic to triage which patients to treat. The question then remains how this would be used and validated in clinical practice.

Example 2: The Right Assessment Measure – the endpoints studied in clinical trials need to be relevant for all stakeholders and can impact the timing and robustness of decisions, regulatory evaluation, patient comfort, time and cost.
In Parkinson's Disease, the motor scale of the Unified Parkinson's Disease Rating Scale (UPDRS) has traditionally been used as the primary outcome for regulatory purposes. This is based on clinician assessment at scheduled visits. Regulators are open to considering other endpoints such as actigraphy (using a motion-sensing device worn by the patient to measure physical activity), This is important, because the use of big data from such digital health endpoints could provide gains in precision, reduction in clinical trial size and faster regulatory approval and patient access. However, such endpoints need to be validated and the form of validation agreed. Is a human factors studies needed or is a simpler evaluation sufficient e.g., evaluating the outcome produced by the technology?

Example 3: Drug+ App - to provide additional benefits for patients through use of non-medicine-based solutions.
In atopic dermatitis and multiple sclerosis, the approaches required for clinical development are well established. The Drug+ approach adds a phone app to capture the clinical progress of the patient in terms of new episodes, relapse, or symptoms for patient to visualize. It is hoped that the combination of a medicine and the app would benefit the patient. However, it is unclear how this should be evaluated and evaluating it like a combination therapy would be very cumbersome.

Challenges with assessment of digital health technologies

Wherever digital technologies are used, many challenges occur. They often produce a large volume of data, but the quality (including completeness and bias) may be poorer than with more traditional forms of data collection. There needs to be seamless data sharing (across systems, groups, organisations), but data privacy and security considerations are increasingly complex. AI and machine learning is still a developing field with questions about black box algorithms, ethics, replicability and validation. Regulatory bodies are now open to dialogue about issues, but as their experience in the field is limited, many conversations may be required to agree appropriate approaches. There is a need for regulatory and HTA bodies to expedite development of their evaluation processes for digital health technologies and harmonize approaches where possible.

Innovation using digital technologies to substitute or add measurements to improve patient diagnosis and assessment will continue at a fast pace. However, there are methodological challenges. Traditional approaches will be too cumbersome if it is expected that the value of the medicine and the associated digital health technology must be both fully demonstrated. It is accepted that scientific rigor is essential to ensure robustness, but a full double demonstration of value is a showstopper for many developers. Furthermore, as R&D takes place in a global setting and various stakeholder develop their learnings, there is a need for consistency in approaches across geographies and decision-makers.

3. Hospital Evaluation of Digital Health Technologies – How is it Different? Professor Kristian Kidholm, Professor of Innovation and Head of Research at the Center for Innovative Medical Technology, Odense University Hospital and the University of Southern Denmark.

Professor Kidholm presented how evaluation of digital health technologies differs from other technologies, drawing on his experience of assessing digital health services/telemedicine over the past decade in a hospital region.

Hospital-based evaluation of telemedicine

The Odense University Hospital uses a range of digital technologies, and their use has increased during the Covid-19 pandemic.

So-called telemedicine is apparent in the more than 300 apps that have been developed by the hospital for different patient groups, with video consultation being used for many patients. Patient reported outcomes (PROs) are sent in from patients in their homes and used by clinicians for monitoring purposes. Point of care testing is being used, for example to measure blood glucose at the bedside or in a patient's own home and this can be combined with apps to manage the patient's condition. There is growth in the number of wearables that provide health information and increasing use of digital robots for logistic tasks (such as transferring goods) around the hospital. AI is a growing field with a large number of new research projects, but it has not yet been used in the treatment of patients in the Odense University Hospital.

To evaluate new digital health technologies, the Southern Denmark region uses the Model for Assessment of Telemedicine (MAST)[1], which is based on the EUnetHTA Core Model® and involves three stages.

I. Prior to the assessment, ensure that the technology and organization is matured and ready for implementation.
II. Multidisciplinary assessment via seven domains:
    1. Health problem and characteristics of the application
    2. Safety
    3. Clinical effectiveness
    4. Patient perspectives
    5. Economic aspects
    6. Organisational aspects
    7. Socio-cultural, ethical and legal aspects.
III. Transferability assessment.

Experience has shown many assessments of telemedicine technologies, where despite the existence of randomized controlled trials (RCTs) undertaken in Denmark or Finland, no impact on quality of life or clinical outcomes has been demonstrated, alongside a substantial increase in costs. For example, home monitoring for chronic obstructive pulmonary disease (COPD), included an RCT of 266 patients, but did not show any impact on hospital admissions or mortality, but was associated with a substantial increase in costs (Sorknaes et al, 2013). Home monitoring for congestive heart failure (CHF) and diabetes was studied in an RCT with 517 patients, but showed no impact on Quality Adjusted Life Years (QALYs) or clinical outcomes (Vuorinen, 2015). Another RCT in 302 patients with diabetes, COPD or CHF found no impact of home monitoring on QALYs but increased costs (Manrey, 2017).

[1] (Kidholm et al 2012) Int J Technol Assess Health Care, 44-51. doi: 10.1017/S0266462311000638
(Kidholm et al 2017) J Telemed Telecare. 803-813. doi: 10.1177/1357633X17721815
(Kidholm et al 2018) J Telemed Telecare. 118-125. doi: 10.1177/1357633X16686553

Likewise, another RCT in 150 patients with COPD found that case management and home monitoring had no impact on QALYs but increased costs.

Lessons learned in evaluation of telemedicine

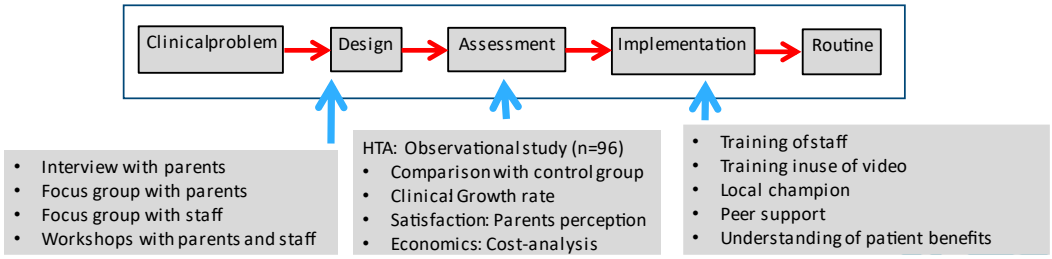
Experience in Southern Denmark provides three key lessons about the evaluation of telemedicine.

Lesson 1. Consider the whole innovation process – do not just focus on assessment.

1) Outline the clinical problem (e.g., large number of outpatient visits or readmissions).
2) Design a solution with full involvement of staff and patients to explain the issues and ensure they will be willing to use the proposed telemedicine service.
3) Assessment via primary HTA research.
4) Implementation using a scientific, participatory approach.
5) Routine use.

An example is shown in Figure 1 for evaluation of home monitoring of premature infants, including video communication with parents to determine if babies aged 4-6 weeks could be sent home safely. The service was designed with the parents and staff, then primary HTA research was undertaken in the form of an observational trial with a historical control. This showed that the growth rate for those treated at home was the same as those treated in the hospital and there was a large reduction in costs. To implement the new service, staff were trained how to do the video consultation.

Figure 1. Consideration of the whole innovation process – Home monitoring of premature infants (KG Holm)



Lesson 2. Use the right primary outcome – patients' perspectives may be most important.
Many telemedicine assessments use a traditional HTA lens and focus on clinical effectiveness, but this may not be most appropriate. Telemedicine often has important long-term impacts on the lives of patients with chronic diseases in terms of empowerment, ability to undertake activities of daily living, reduced time and travel for hospital visits and changing the patient-doctor relationship. It could be that clinical outcomes may not improve with telemedicine, but improvement in these aspects may still be highly valuable and so care must be taken to design studies that can capture the aspects that patients deem to be important. If there is a focus only on the clinical outcomes, the true value of a telemedicine service may be missed.

Lesson 3. Use the right research design.
RCTs are not always needed to evaluate clinical information systems. Liu and Wyatt (2011) highlighted that the design should be driven by the expected health impact and costs of the system. Technologies that are expected to be high cost and potentially have major clinical impact require an RCT to assess clinical outcomes, safety and costs. Whereas, for example, apps that are low cost, which are not expected to impact on clinical outcomes may only need a small patient satisfaction survey.

4. Digital Health Interventions – Evidence Needed, Methods and Assessment for Policy Decisions – Perspectives from a National HTA Body

Jeanette Kusel, Director for Scientific Advice, National Institute for Health and Care Excellence, England

Jeanette Kusel gave an overview of the process for evaluating digital health technologies at the National Institute for Health and Care Excellence (NICE) in England. She gave insights from her experience in scientific advice dialogues with companies about the development of clinical and economic evidence for HTA of digital health technologies and in establishing the new office for digital health at NICE.

Evaluation of digital health technologies at NICE

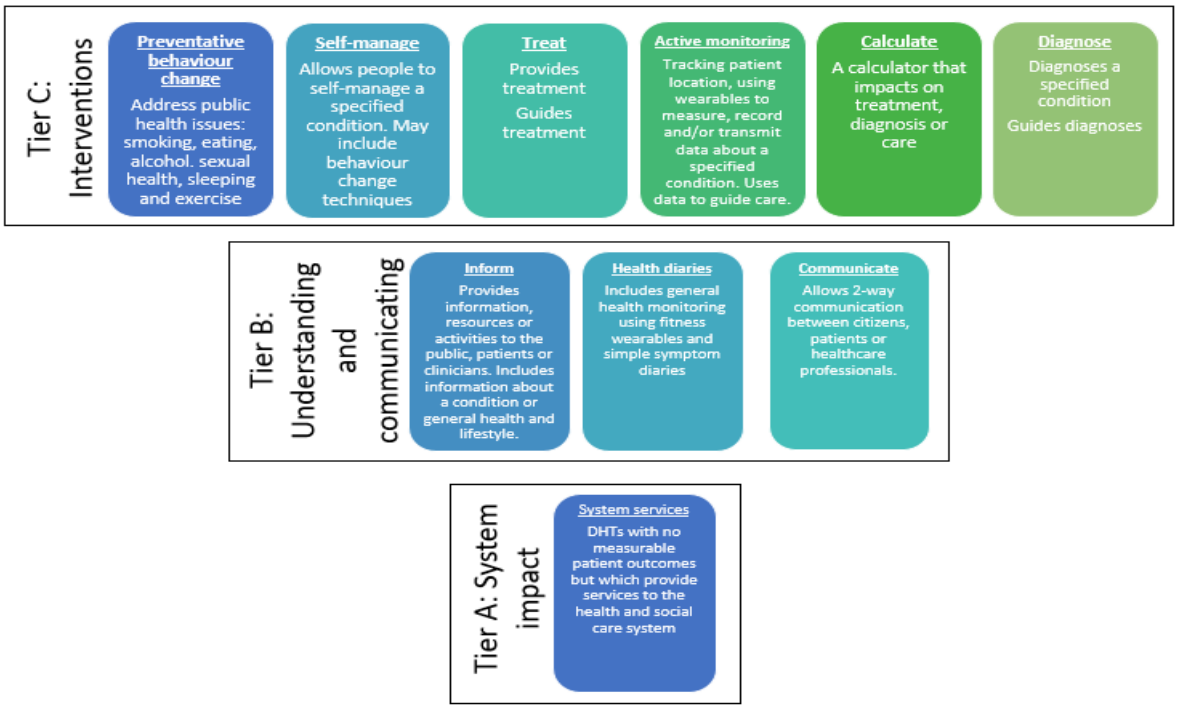
The new five-year strategy for NICE outlines its aims to provide leadership on the evaluation of the value of digital health technologies. This will include provision of best practice guidance and quality standards for digital health technology evidence and evaluation methods. Furthermore, to ensure a streamlined path from development to use, NICE will work with health system partners to provide clarity on the regulation and commissioning of digital health technologies.

Digital health technologies do not have a separate evaluation programme at NICE, but are assessed via the most appropriate NICE programme, depending on the nature of the technology (diagnostic technologies, medical technologies etc) and whether the technology is likely to increase or reduce health or social care spending. Thus, existing methods will be used as the basis for producing guidance.

Evidence standards framework for digital health technologies

NICE has recently updated its evidence standards framework for digital technologies which includes three tiers according to the functionality and associated risk of the technology (Figure 2). This enables definition of proportionate evidence requirements for technologies from the low-risk system technologies to more complex, high-risk technologies that might be used for diagnosis or treatment of a patient. The Evidence Standards Framework has been designed to allow commissioners to understand ‘what good looks like’ in digital health technologies and to help developers to understand what kind of evidence they need to generate. This framework will be extended in future to include complex AI technologies.

Figure 2. NICE Evidence Standards Framework for Digital Health Technologies



HTA methods for digital health technology evaluation – challenges, pilots and conclusions

HTA questions for AI

AI provides a good example of the challenges faced by HTA in evaluating digital health technologies. AI requires conceptualization of the algorithm, algorithm training, validation and clinical investigation. HTA needs to assess each step, with questions such as the following:

Algorithm training
- ? what dataset was used for the algorithm training
- ? is the training dataset generalizable to the population in the health system
- ? is it high quality and complete
- ? are data labelled accurately
- ? is it unbiased.

Validation
- ? is it generalizable
- ? can it be applied to the entire population that may come forward in the health system.

Clinical investigation
- ? how will the digital technology be used in clinical practice, e.g., is it always followed, or when will clinicians over-ride the algorithm.
  (This is often overlooked in evidence generation plans, but is important to understand the impact of the technology on the clinical pathway and resource use).

Furthermore, continuous monitoring and algorithm learning is inherent in AI, and this poses questions for HTA about how it evaluates a technology it knows is changing, if RWD collection is required, and when guidance should be updated.

NICE pilot in AI

An example of a NICE pilot HTA of an AI technology is that of Zio. Zio is an ECG monitoring technology for detecting cardiac arrhythmias, which is CE marked as Class IIa. It incorporates a device that is attached to the chest and AI software monitors the heart rhythm, and signals when there may be an arrhythmia. In the pilot appraisal of Zio, NICE sought advice not only from clinical experts, but also from AI experts and a patient survey was undertaken, alongside a standard critical assessment by an academic group. There was a substantial clinical evidence base with 17 studies (four of which were comparative, 12 were single arm). These studies were somewhat different to the usual clinical studies reviewed, but it was still possible to review bias and generalizability. The economic evidence presented cost modelling, with separate cardiology and stroke models with a downstream model (to 1 year) for stroke patients. In the committee appraisal discussion, the technical data relating to diagnostic accuracy from validation studies was accepted. Similarly, the use of AI in the technology ("within the black box") and conformity with NHS data standards was deemed acceptable. The main issues that arose were those common with other health technologies, namely the resource use assumptions in the economic modelling and the determination of longer-term clinical outcomes. Overall, the HTA was positive but recommended collection of more data on healthcare resource use and long-term clinical outcomes.

HTA methods for digital health technologies

Considering whether current HTA approaches are fit for appraising digital health technologies, there are three areas of consideration, where:

1. Existing HTA methods are applicable
   (Digital health technologies are often developed rapidly, there are specific concerns about bias and disruption to care pathways.)
   i) existing HTA methods can deal with the uncertainty that arises from a limited evidence base
   ii) there are also good methods to assess bias and generalizability and
   iii) HTA can help determine the place of technology in the care pathway.

2. New HTA skills are required
   i) interpretation of internal and external validation results
   ii) knowing how much of the "black box" of the algorithm needs to be understood given the clinical effectiveness outcomes
   iii) recognizing what can be left to others such as the regulator and other advisers to the health system about digital technologies. (For example, in England, Digital Technology Assessment Criteria have been established by NHSX and this will include issues such as technical interoperability.) So, it is important that HTA focuses on assessment of issues that will not be considered elsewhere in the health system.

3. More work is required
   i) the evidence submitted about the training and validation datasets needs to be improved to better present the demographics of those studied and the quality of the dataset.
   ii) consideration needs to be given of how to handle algorithm updates (particularly for adaptive algorithms arising from machine learning (ML)) and whether continuous monitoring is needed, what would trigger review of the HTA and how this will be resourced.

Assessment of digital health technologies is an evolution, not a revolution. There are good tools in the existing HTA toolbox that can be used. As new complex digital health technologies arrive, HTA will need to evolve, but there doesn't need to be a revolution in HTA methods. It will be important to learn as more experience is gained in assessing digital health technologies. Putting this into the context of the life sciences ecosystem, early engagement with decision makers about digital health technologies is crucial, particularly because the developers of digital health technologies are often small startups or larger technology companies that don't have a good understanding of the evidence requirements and methods for HTA.

5. Digital Health Interventions – Evidence Needed, Methods and Assessment for Policy Decisions: Experiences and Reflections from the Asian Region

Professor Ying Yao Chen. Professor of Health Services at the School of Public Health and Director of the Key Lab of HTA, Fudan University and Director of WHO Collaborating Center of HTA and Management

Professor Chen reflected on the status of digital health in the Asian region and challenges of assessment.

International landscape for digital health

The draft World Health Organization Global Strategy 2020-2024 refers to "digital health" as "the field of knowledge and practice associated with the development and use of digital technologies to improve health". It encompasses mobile health (mHealth), eHealth, telemedicine, and advanced computing sciences like genomics, artificial intelligence (AI), and big data. Digital health has been highlighted as a way of realizing precision medicine, and in addition is expected to become synonymous with health itself with the rapid digitization of all health-related data.

The Riyadh Global Digital Health Summit in 2020 was a landmark international forum that highlighted the importance of digital technology, data, and innovation for resilient global health and care systems. It developed the Riyadh Declaration[2] that calls on the global health community to **"create the infrastructure needed to share effective digital health evidence-based practices and high-quality, real-time data locally and globally to provide actionable information to more health systems and countries"**.

Current status of digital health in Korea, Pakistan and China

With this clear policy imperative, a rapid literature review was undertaken searching for the terms 'digital health interventions' or 'digital health technologies' in Pubmed in English and CNKI in Chinese. One hundred and twenty-two relevant studies were identified. Most studies were found in the Journal of Medical Internet Research and its sister journal JMIR mhealth and uhealth. Examples to show diversity in countries and across conditions are presented for Korea, Pakistan and China covering use of digital health technologies in Covid-19, chronic disease and hospital management.

Based on rapid technological advancements, Korea is shifting focus from hospital information systems to medical AI (Shin, 2019[3]). Many companies are developing medical AI technologies and six have been approved by the Korean Ministry of Food and Drug Safety

[2] Al Knawy B, Adil M, Crooks G, Rhee K, Bates D, Jokhdar H, et al. The Riyadh Declaration: the role of digital health in fighting pandemics. Lancet 2020;396(10262):1537-9.

[3] Shin SY. Current status and future direction of digital health in Korea. Korean J Physiol Pharmacol. 2019 Sep;23(5):311-315.

(regulatory agency). This compares with 20 approvals by the US Food and Drug Administration and 17 CE approvals in the EU. The majority of the approved medical AI solutions in Korea are for Picture Archiving and Communication Systems (PACS) providing computer-aided diagnosis of radiology images.

Due to resource constraints, the current infrastructure of Pakistan struggles to provide access to high-speed internet and smartphones to two-thirds of its population and this inhibits the use of digital health technologies (Kazi, 2020[4]). The high cost of establishing technology-based interventions, including both human resources and infrastructure costs (software and hardware), is a major barrier in Pakistan and this is typical of other low- and middle-income counties and must be recognized.

To describe the situation in China, three examples are presented:

1. Digital epidemiology for investigating the Covid-19 outbreak – two examples.
2. The effect of smartphone app–based interventions for patients with hypertension.

The first two examples relate to contact tracing of individuals with Covid-19 (He, 2020[5]). Each start with one individual patient. The first example used mobile phone carrier's tracking systems and scrutinized the data transmission between different base stations. The patient was diagnosed on 1 February 2020 and known to have recently returned from Wuhan. It was identified that he had 3557 people as general contacts and eight of these were confirmed as having infections. Strict measures were then undertaken: the 8 confirmed cases and 2 suspected cases were admitted to hospital to receive treatment, 52 close contacts were observed in intensive medical quarantine, 91 key subjects received home medical observation, and all 3557 general contacts were followed up and monitored.

The second case related to an individual diagnosed in early February 2020 who had not been to an infected area or obviously exposed. After referring to community surveillance cameras, it was determined that the patient had spent a short period standing near a stranger in a booth at a farmer's market 11 days earlier. The stranger was not wearing a mask and was a confirmed case. Using video surveillance, the whereabouts of this patient were retrieved, which resulted in the identification of 19 subjects with close contact, who were then put under observation in designated hospitals to prevent further contamination.

These two publicly reported cases demonstrated the important role that digital data can have in modernizing epidemiological investigation and their potential to guide public health measures.

A different example relates to self-management of a long-term condition, namely hypertension (Xu, 2020[6]). Lifestyle changes such as dietary sodium restriction, weight loss, and aerobic exercise can substantially decrease blood pressure. Smartphone apps could offer a tool to provide reminders to take medication, track biometric results, support lifestyle management and behavior change through education, motivation and individualized coaching based on values and behaviors. When combined with regular blood pressure monitoring, systematic reviews demonstrate the added benefit of these apps in terms of adherence, adherence+physical activity and blood pressure reduction compared with non-digital hypertension management strategies. However, these analyses also showed

[4] Kazi AM. Current Challenges of Digital Health Interventions in Pakistan: Mixed Methods Analysis. J Med Internet Res. 2020;22(9):e21691

[5] He Z. A New Era of Epidemiology: Digital Epidemiology for Investigating the COVID-19 Outbreak in China. J Med Internet Res. 2020;22(9):e21685

[6] Xu H, Long H. The Effect of Smartphone App-Based Interventions for Patients With Hypertension: Systematic Review and Meta-Analysis. JMIR Mhealth Uhealth. 2020 Oct 19;8(10):e21759

heterogeneity, which is an important consideration with digital technologies – that they may work in some patients, but not others.

Challenges assessing digital health technologies [7]:

The Covid-19 context

- Many digital health solutions for Covid-19 are being rapidly deployed to health service consumers without rigorous evaluation of their safety, effectiveness and ethical issues. HTA of these interventions could help identify issues and mitigate risks before they may have adverse consequences for patient safety and organisational functioning.
- Use of digital technologies can speed up the identification of exposed individuals for testing and quarantine, the risks of digital contact tracing including safety and privacy concerns need to be monitored and managed.
- Digital contact tracing solutions could breach privacy; may result in false alerts or fail to detect individuals if mobile devices are turned off or lose connectivity.

Appropriate evaluation over the life cycle

- Many digital health technologies are being developed and shared at a faster rate than they can be assessed, presenting patients and clinicians with the challenge of distinguishing helpful tools from harmful ones.
- Evaluation is needed at each distinct stage in the digital health technology lifecycle including design, development, selection, implementation, use, and ongoing surveillance.
- As the digital health technology moves through its lifecycle, the focus of evaluation changes from a formative assessment —which is focused on shaping the design of an intervention (such as digital contact tracing) and tends to be lightweight, inexpensive and quick. Later in the life cycle a summative assessment is required that rigorously determines whether the intervention, once in use, actually achieves the intended outcomes.
- The methods used to evaluate digital health technology must take account of the technology and use, and be scientifically robust, for example with a clear protocol. For instance, rapid usability testing can be used to refine the design of a digital contact tracing app, while the effectiveness of digital contact tracing over manual methods will require a rigorous approach to measure speed and accuracy.
- Given rapid product cycles and frequent updates, even the most thorough evaluation is only as accurate as the data it is based on. It requires real-world data on the actual use, effects, benefits, and harms of these digital health tools.

In conclusion, HTA is not used sufficiently to evaluate digital health technologies and need to address the challenges associated with this rapidly evolving and developing technology sector. HTA of digital health technologies needs to address not only outcomes, but also structure and processes including perspectives from hospitals, patients, payers, etc. This field urgently needs development of data and methodologies, which could be achieved through enhanced collaboration. In such collaborations, it is important to recognise that the current state of development of health technologies and capacities are diverse across Asia, and they have different priorities.

[7] Magrabi F. Managing Pandemic Responses with Health Informatics - Challenges for Assessing Digital Health Technologies. Yearb Med Inform. 2021 Apr 21.
Rodriguez-Villa E. Regulating digital health technologies with transparency: the case for dynamic and multi-stakeholder evaluation. BMC Med. 2019 Dec 3;17(1):226.
Solomon DH, Rudin RS. Digital health technologies: opportunities and challenges in rheumatology. Nat Rev Rheumatol. 2020 Sep;16(9):525-535.

6. Discussion with audience

Dr Sampietro-Colom thanked the panelists for their insightful contributions about HTA considerations when assessing digital health interventions. She issued the next poll question and invited questions from the audience.

Poll question 2
Which domains from the EUnetHTA and AdHopHTA frameworks are most relevant for digital health interventions (select 3 most important)?

D1: Health problem and current use
D2: Description and technical characteristics
D3: Safety aspects
D4: Clinical effectiveness
D5: Costs and economic evaluation
D6: Ethical aspects
D7: Organisational aspects
D8: Patient and social aspects
D9: Legal aspects
D10: Political and strategic aspects

The three most relevant domains for assessment of digital health technologies are considered to be clinical effectiveness, description/technical characteristics and patient and social aspects.

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Question (Anke Peggy Holtorf, Outcomes Consultancy, Switzerland): Given the continuous updating of the algorithm in AI applications, how frequently would an assessment have to be revised and what other monitoring mechanisms to ensure continuing effectiveness could be used?

JK: We don't have the answers yet, but we can take learnings from assessments of medical devices, as they too evolve quickly, and we have to determine when to re-assess them. However, this evolution is faster for digital health technologies, so we need to think about this further, particularly the potential to use other monitoring mechanisms. Could other technology be used to help monitor the digital health technology? Particularly for adaptive algorithms, how can software be used to take the data generated by adaptive algorithms and monitor in a way that saves human resources.

KK: In our mid-size hospital with 1,100 beds and staff of 12,000 people we have 100s of new digital services coming into operation and this will grow in the future. It is a major challenge to do the initial assessment of a digital health technology. It seems unrealistic to be expected to do rapid HTA evaluations of updated algorithms and perhaps a national organisation could help with this. Prioritization of HTA resources is important to consider as not all digital health technologies are subject to HTA. Perhaps we need to focus on appropriate use of HTA for the most important digital health technologies, e.g., technologies with high costs or potential large clinical consequences.

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Question (Ed Clifton, Non-Medicines HTA Body, Scotland): At NICE, the importance of bespoke evaluation of digital health technologies including issues such as algorithm training and validation was noted, but it was explained that there isn't a bespoke committee for appraisal of digital health technologies. Does this mean that the role of the academic groups to critically assess the evidence is more important?

JK: When NICE committees appraise these technologies for the first time, they are more reliant on the technical assessments from the academic groups. This is likely to continue for some time and there is a need to train committees. However, this really only relates to the more complex digital health technologies that involve AI algorithms to inform clinical decision making. There are many digital health technologies that are much simpler and easier to appraise.

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Question (Karen Facey, Non-Medicines HTA Appraisal Committee, Scotland): There has been hesitancy in uptake of AI due to the black box nature of the algorithms, which may vary across manufacturers and so clinicians don't trust them. Is it possible to demystify the algorithms to enable expert clinical review to judge against standard clinical practice?

YY: Clinician involvement in the development and assessment of digital health interventions to compare to current best standard of care is essential. This would not only improve development, but also increase the trust of clinicians.

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Question (Meindert Boysen, HTA body, England and Wales): What aspects of value frameworks need to change when making decisions about the introduction of digital health technologies? We might be confident about applying current HTA approaches, but do we know what our customers want from HTA, especially if the customers are patients?

KK: This was evaluated in the EU AdHopHTA project. We interviewed hospital managers to identify what was important to them when making decisions about health technologies in general. This showed that clinical outcomes and economic issues were most important for their decisions.
When I talk to clinical departments about digital health services, they want evidence about how it will affect their practice. As indicated in my presentation, there is a paucity of evidence relating to the clinical outcomes associated with use of digital health technologies, but patients value a range of other things like reduced travel requirements, they feel more empowered with the ability to self-test and learn what to look for to better manage their condition. This new role for the patient of being active in disease management and being able to talk with the clinician via video to develop shared decision-making are all very important outcomes to many patients with chronic diseases and helps them to become expert patients. So perhaps clinical improvement is not so important, but changes in the patient's perception and ability to live their life fully with a chronic disease are.

JK: As Professor Kidholm indicated, it's important to consider what patients want from digital health interventions. At NICE, there is a new programme called "NICE listens", which will involve the public and patients to understand their views about trade-offs. AI is one area we will be discussing with them.
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Question: How do we ensure AI doesn't perpetuate health inequalities?

JK: There are several ways AI could perpetuate health inequalities. Older patients may not have access to smartphones, to overcome this, there needs to be alternative ways of access.
If the algorithm is biased, HTA can consider this explicitly in its assessment.

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Poll question 3 (repeating question 1):
Are we ready to assess digital health technologies with our current HTA methods?
Yes 47%
No 47%
Unsure 6%.

So given the discussion of this panel more people now consider HTA is ready to assess digital health technologies, but there is clearly some work to do to develop processes further.

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In conclusion, Dr Sampietro-Colom summarized that HTA methods are suitable to evaluate digital health technologies, but these need to be evolved and consideration given to the most important outcomes for assessment. Given the rapid development of digital health technologies, it would be interesting to see how the panellists have innovated HTA to handle digital health technologies at the HTAi conference in 2022.